REMARKS

Claims 1-5 are pending in the case and Claims 1-5 are rejected under both 35 USC 112 (second paragraph) and 35 USC 103(a) (in light of Whitaker). With this response, new dependent Claims 10 and 11 have been added.

REJECTIONS UNDER 35 USC 112 (Second Paragraph)

Claims 1-5 are rejected under section 112, second paragraph. The office action states that the term "inoculation well" is unclear as to what the structural limitations of the phrase are. The office advises that the language of a claim must make clear what the subject matter of the claim encompasses, so as to delineate its "metes and bounds."

Applicants assert that the inventive inoculation well is fully described to a skilled practitioner in the art, and applicants provide the following support for their position. Applicants also assert that the description of the "inoculation well" presented in the specification and identified in the claims is fully consistent with the requirement of Section 112, second paragraph.

MPEP § 2173.05(a) New Terminology

THE MEANING OF EVERY TERM SHOULD BE APPARENT

The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed. Applicants need not confine themselves to the terminology used in the prior art, but are required to make clear and precise the terms that are used to define the invention whereby the metes and bounds of the claimed invention can be ascertained. During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. *In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969).

The requirements for clarity and precision must be balanced with the limitations of the language and the science. If the claims, read in light of the specification, reasonably

apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the statute (35 U.S.C. 112, second paragraph) demands no more. *Shatterproof Glass Corp. v. Libbey Owens Ford Co.*, 758 F.2d 613, 225 USPQ 634 (Fed. Cir. 1985) ... If the proposed language is not considered as precise as the subject matter permits, the examiner should provide reasons to support the conclusion of indefiniteness and is encouraged to suggest alternatives that are free from objection.

MPEP § 2173.05(g) Functional Limitations

A functional limitation is an attempt to define something by what it does, rather than by what it is (e.g., as evidenced by its specific structure or specific ingredients). There is nothing inherently wrong with defining some part of an invention in functional terms. Functional language does not, in and of itself, render a claim improper. In re Swinehart, 439 F.2d 210, 169 USPQ 226 (CCPA 1971).

A functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. A functional limitation is often used in association with an element, ingredient, or step of a process to define a particular capability or purpose that is served by the recited element, ingredient or step. Whether or not the functional limitation complies with 35 U.S.C. 112, second paragraph is a different issue from whether the limitation is properly supported under 35 U.S.C. 112, first paragraph or is distinguished over the prior art.

RESPONSE:

The term "inoculation well" is defined throughout the specification in both functional and specific terms. Relevant sections of the specification include:

a) on page 3 of the specification, it states: "Our novel inoculation bioreactor is designed to facilitate an improved method of mammalian cell seed-train expansion, and is distinguished by the presence of *an "inoculation well" which communicates with the interior of the bioreactor and which facilitates the growth of mammalian cells for commercial seed-train expansion*."

b) on page 3 of the specification, in the description of the preferred embodiment, the inoculation bioreactor is described as *having an "inoculation well" located at the base of the reactor chamber*. The *inoculation well is supplied with fermentation sensors (pH, dissolved oxygen, temperature, optical density, etc.) to assist in assuring optimal cultivation conditions. Most preferably, this inoculation well is adapted to include an impeller drive* ... .

c) on page 7 of the specification, the two different bioreactors that were evaluated had *inoculation wells had 2 liter volume*. The two bioreactors were of 7L and 15L volumetric sizes respectively, and the size ratio of bioreactor volume to inoculation well volume can readily be determined.

d) on page 4 of the specification, in the Brief Description Of The Figures, *Figure 3 is identified as showing the concept of the "inoculation well"* inoculation bioreactor. This figure clearly shows that three monitoring probes (temp, pH, and pO) are directed to the inoculation well, and the well is identified as being of a 2L volume, and located at the base of the bioreactor.

e) on page 9 of the specification, the inoculation well is described as follows: "*The inoculation well of the bioreactor will normally be small (in the present examples a 2L inoculation well was used) and the volume may be increased by increasing the diameter and the height of the bioreactor. Since* $V_{IR\ max}$ *is not limiting, the same "inoculation well" concept can be applied to the design of larger bioreactors.* (see figure 3)."

Taken together, descriptions "a" through "e" provide: a design for both the inoculation bioreactor and inoculation well, representative volumes for the inoculation well, a formula to use in scaling the size of the inoculation well to the size of a bioreactor, location of the inoculation well relative to the inoculation bioreactor, environmental

probes used to monitor the environment within the inoculation well, and demonstration sizes of both the inoculation well and bioreactor. Skilled practitioners in this art will know from reading the specification what materials should be used to build the inoculation bioreactor. In summary, all essential features of the inoculation well have been fully provided. Details of the method of seed train expansion which employ the inoculation well is described in detail in paragraph 3, page 3 of the specification.

As discussed above, applicants assert that all necessary features of the inoculation well have been fully described (especially to a person skilled in the art). In light of the amendment to the claims, that serve to describe the method is additional detail, and the information provided above, applicants respectfully request the Patent Office to reconsider and withdraw this basis of rejection.

REJECTIONS UNDER 35 USC 103(a)

Claims 1-5 are rejected under 35 USC 103(a) in light of Whitaker et al. The Office Action alledges that Whitaker teaches seed train expansion from cryopreserved samples, while cell growth is monitored and optimized. The Office Action also states that the distinct feature of the invention appears to be the "inoculation well" and that the broadest reasonable interpretation of "inoculation well" would appear to encompass the section of the bioreactor of Whitaker which holds the cells and medium.

Applicants traverse the argument presented by the Office, and assert that the method of seed train expansion presented in amended claims 1 - 5 and new claims 10 and 11 are very substantially different from the technology disclosed by Whitaker. In addition, the basis of rejection presented by the Office does not fall within the requirements established by the Supreme court in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). By suggesting that applicants' invention is encompassed in the bioreactor of Whitaker impermissibly disregards the requirement to analyze the subject matter as a

whole. **Distilling an invention down to the "gist" or "thrust" of an invention disregards the requirement of analyzing the subject matter "as a whole."** *W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984)*

The use of the inoculation well presented and claimed in applicants' pending application allows mammalian cell seed train expansion to proceed directly from the inoculation culture (e.g. cryopreservation bag) into the bioreactor. As is described in the Background section on Page 1, cell culture expansion in the disclosed invention is done completely in the bioreactor, which eliminates multiple cell transfers and the accompanying sources of potential contamination. The Whitaker chapter describes the procedure commonly used in the industry for expanding cell cultures (depicted in Figure 1, "Process Overview") and separately, the operation of a high volume perfusion bioreactor. **Please note**, the operation of the **high** volume (500L) perfusion bioreactor (described by Whitaker on page 28) begins with the addition of a 50L culture. The 50 L perfusion bioreactor is according the Whitaker fed by cells that have been expanded by the process shown in Figure 1. Figure 1 has six steps: 1) Providing a frozen vial of cell bank, 2) transferring the cells to small T-flasks, 3) then after a period of time retransfer to large T-flasks, 4) then the culture is moved to a small Spinner Flask, 5) then it's transferred to a larger Spinner Flask, and 6) finally its finally transferred to a Bioreactor (or even a perfusion bioreactor). Every time the cells are transferred from one vessel to another, opportunities for contamination are encountered. (See background section [page 1] of applicants application). Applicants' invention provides a system for expanding cells directly from a cryopreserved container (e.g. cryopreservation vial or bag) to a larger volume while avoiding the problems associated with the multiple cell transfers required by the prior art. The inventive inoculation well enables the claimed process of cell expansion to occur, without having to employ all the intermediate steps described in Figure 1 of Whitaker, while at the same time accomplishing the same goal. In short, the inventive process eliminates multiple intermediate steps but retains the same functionality. **(Note that the omission of an element and retention of its function is**

an indicia of unobviousness. *In re Edge, 359 F.2d 896, 149 USPQ 556 (CCPA 1966) MPEP 2144.04*))

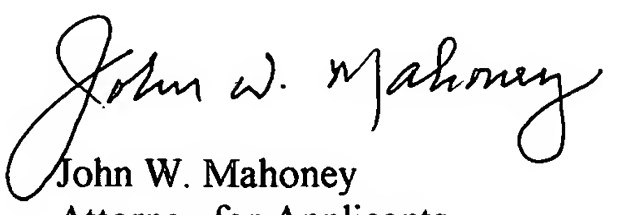
From the discussion presented above, it will be seen that the bioreactor of Whitaker does not provide the same functionality as the inoculation well disclosed by applicants. (Whitaker is obviously an expert in this field, and had he thought that the steps shown in Figure 1 could be eliminated by the use of his bioreactor, he would have done so.) Accordingly, applicants respectfully request that the Patent Office reconsider and withdraw this rejection under §103.

Applicants believe that the pending application and claims are in condition for allowance, and early grant of allowance is earnestly requested.

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Examiner is encouraged to call Applicants' Attorney at the phone number listed below.

Applicant's attorney expresses his appreciation to the Examiner for examining this application. Thank you.

Respectfully Submitted,



John W. Mahoney
Attorney for Applicants
Reg. No. 44,892

Bayer Corporation
(510) 705-7725